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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/691,711	10/23/2003	Rolf Banholzer	1/1148-2-C2	2056
28501 7590 11/02/2007 MICHAEL P. MORRIS BOEHRINGER INGELHEIM CORPORATION 900 RIDGEBURY ROAD P. O. BOX 368 RIDGEFIELD, CT 06877-0368			EXAMINER COPPINS, JANET L	
			ART UNIT 1626	PAPER NUMBER
			MAIL DATE 11/02/2007	DELIVERY MODE PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

## Office Action Summary

Application No.

10/691,711

Applicant(s)

BANHOLZER ET AL.

Examiner

Janet L. Coppins

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 08 August 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-4 and 9-21 is/are pending in the application.
- 4a) Of the above claim(s) 17-21 is/are withdrawn from consideration.
- 5) ☒ Claim(s) 1-4 and 9-15 is/are allowed.
- 6) ☒ Claim(s) 16 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_

### **DETAILED ACTION**

1. Claims 1-4 and 9-21 are currently pending in the instant application.

#### ***Response to Amendment***

2. Applicants' Amendment and Response of August 8, 2007, has been reviewed by the Examiner and entered of record in the file. Accordingly, claim 2 has been amended.

#### ***Terminal Disclaimer***

3. The terminal disclaimer filed on August 8, 2007, disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of U.S. 6,777,423 B2 has been reviewed and is accepted. The terminal disclaimer has been recorded.

#### ***Claim Rejections - 35 USC § 112***

4. Claims 1-4 previously rejected under 35 U.S.C. 112, first paragraph, as not being enabled. In view of Applicant's persuasive arguments and amendments to the claims, the Examiner withdraws the rejections to claims 1-4.

#### ***Double Patenting***

5. Claims 1-4 previously rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-6 of U.S. Patent No. 6,777,423 B2. Applicants' Terminal Disclaimer, submitted August 8, 2007 (please see above) is sufficient to overcome this rejection.

#### ***Rejoinder***

6. Claims 1-4 now directed to an allowable product. Pursuant to the procedures set forth in MPEP § 821.04(b), claims 9-16, directed to the process of making the allowable product and its pharmaceutical composition, previously withdrawn from consideration as a result of a restriction

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requirement, are hereby **rejoined** and fully examined for patentability under 37 CFR 1.104.

Claims 17-21, directed to the invention(s) of Groups IV-V, have NOT been rejoined.

Because a claimed invention previously withdrawn from consideration under 37 CFR 1.142 has been rejoined, **the restriction requirement between groups I-III as set forth in the Office action mailed on October 27, 2006 is hereby withdrawn.** In view of the withdrawal of the restriction requirement as to the rejoined inventions, applicant(s) are advised that if any claim presented in a continuation or divisional application is anticipated by, or includes all the limitations of, a claim that is allowable in the present application, such claim may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Once the restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. See *In re Ziegler*, 443 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

***New Claim Rejections-***

***35 USC § 112***

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claim 16 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the crystalline form of tiotropium bromide monohydrate, does not reasonably provide enablement for a pharmaceutical composition containing said form. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to prepare the invention commensurate in scope with these claims.

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In *In re Wands*, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in the previous Office Action.

***The nature of the invention***

The nature of the invention is a crystalline monohydrate form of tiotropium bromide in a pharmaceutical composition.

***The state of the prior art and the predictability or lack thereof in the art***

It is the state of the prior art that polymorphism is the existence of different solid forms (modifications) of a compound which have the same chemical composition but different structures and thus different physical and sometimes also chemical properties (Concise Encyclopedia Chemistry, 1993). It is also the state of the art that any polymorph (including compounds that are characterized by the DSC and IR data in Figures 1 and 2 of the specification) might include other forms without the same X-ray diffraction patterns. It is the state of the prior art that under any given pressure and temperature, other than the conversion points, only one modification is stable, the form with the lowest vapor pressure. Often the conversion rate in the solid phases is so slow that even modifications, which are unstable under normal conditions, can be kept for a long time in their metastable state. This conversion rate can depend on the rate of temperature change or pressure change (Concise Encyclopedia Chemistry 1993). The predictability or lack thereof in the art is that there can be multiple forms of a solid in existence and these polymorphs are created by varying crystallization processes that began with varying starting materials, utilize varying solvents, varying temperatures and varying reaction times.

There is no method that exists to predict the polymorphs of a solid compound with

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significant certainty (Rouhi, page 32). Preparing a crystalline form of any compound will cause a specific crystalline form, if in the metastable state, to always resort back to the most thermodynamically stable form.

Regarding newly rejoined composition claim 16, polymorphs tend to convert from less stable to more stable forms. Dissolving the specific crystalline form in water, creating an aqueous solution, would put the compound in its free form and not in a crystalline form with the specific X-ray diffraction pattern as claimed. In aqueous phases, all physical forms are amorphous. Thus the metastable compound will resort back into its most thermodynamically stable form which would have a different X-ray diffraction pattern and also that a solution prepared from a specific crystalline form and water would contain the free form of the compound. Applicants have provided no evidence to ensure that their crystalline compound will maintain the specific monohydrate form as recited and will not resort back to the free form of the most thermodynamically stable form of the compound while in composition, therefore the claims cannot distinctly point out and claim the intended crystalline monohydrate form.

*The amount of direction or guidance present and  
the presence or absence of working examples*

The only direction or guidance present for the instant composition is the preparation of the specific crystalline forms defined by the data found in Figures 1 and 2 of the instant specification.

*The breadth of the claims*

The breadth of the claims is a pharmaceutical composition allegedly containing a crystalline hydrate of tiotropium bromide.

***The quantity of experimentation needed and the level of the skill in the art***

The quantity of experimentation is extremely high. One would need to prepare crystalline hydrates of tiotropium bromide in composition by many different methods to determine which form would be stable, while the specification only provides methods and direction to the process of the preparation of the specific crystalline forms with the DSC and IR spectra found in Figures 1 and 2 of the instant specification. The level of skill in the polymorph art is high. However, without a showing or guidance as to how to ensure that the specific monohydrate form as claimed remains stable in solution, it would require undue experimentation to figure out how to prepare the pharmaceutical composition with the crystalline monohydrate form as claimed.

9. Claims 1-4 previously rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In view of Applicants' persuasive arguments and amendments to the claims, the indefiniteness rejections are withdrawn.

***Conclusion***

10. In conclusion, claims 1-4 and 9-21 are pending, claims 17-21 are currently withdrawn, and claim 16 is currently rejected. Claims 1-4 and 9-15 appear allowable over the prior art.

***Telephone Inquiry***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet L. Coppins whose telephone number is 571.272.0680. The examiner can normally be reached on M-F 8:30-5:00.

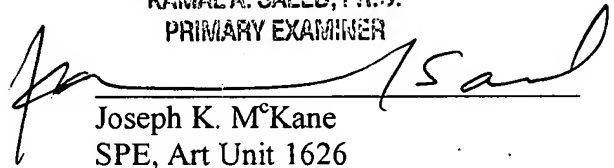
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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph K. McKane can be reached on 571.272.0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Janet L. Coppins  
October 27, 2007

KAMALA SAEED, PH.D.  
PRIMARY EXAMINER



Joseph K. McKane  
SPE, Art Unit 1626